**Citation:**

Giles GG, Simpson JA, English DR, Hodge AM, Gertig DM, Macinnis RJ, Hopper JL. Dietary carbohydrate, fibre, glycaemic index, glycaemic load and the risk of postmenopausal breast cancer. *Int J Cancer.* 2006 Apr 1;118(7):1843-7.

**PubMed ID:** 16217755

**Study Design:**

Prospective Cohort Study

**Class:**

B - Click here for explanation of classification scheme.

**Research Design and Implementation Rating:**

NEUTRAL: See Research Design and Implementation Criteria Checklist below.

**Research Purpose:**

To investigate associations between dietary carbohydrates, glycemic index and glycemic load, and dietary fibre, and risk of invasive breast cancer in a prospective study of post-menopausal women with a wide range of relevant dietary exposures and detailed tumour characteristics.

**Inclusion Criteria:**

- Residents of Melbourne metropolitan area, aged 40 - 69 years
- Migrants from Italy and Greece were deliberately recruited to increase the range of dietary exposures available

**Exclusion Criteria:**

- Subjects with confirmed invasive breast cancer prior to baseline (n = 386 women)
- Pre-menopausal or of unknown menopausal status at baseline (n = 10,374 women)
- Self-reported heart attack, diabetes and angina at baseline (n = 1,446 women)
- Missing data for the food frequency questionnaire or extreme values of total energy intake (<1st percentile and >99th percentile)

**Description of Study Protocol:**

**Recruitment**

In 1990-1994, the Melbourne Collaborative Cohort Study (MCCS) recruited 41,528 people (24,479 women) from the Melbourne metropolitan area. Migrants from Italy and Greece were deliberately recruited to increase the range of dietary exposures available.

**Design:** Prospective Cohort Study

**Blinding used (if applicable):** not applicable

**Intervention (if applicable):** not applicable

**Statistical Analysis**

- Cox proportional hazards regression, with age as the time axis, was used to derive relative risk for each nutrient and food group measured at baseline
- Country of birth and total energy intake were included in all models
- Potential confounders were included in final analyses if they changed the RR of any nutrient by at least 5%

**Data Collection Summary:**

**Timing of Measurements**

Dietary intake assessed at baseline. At interview, questions were asked about reproductive history, country of birth, alcohol intake, physical activity, highest level of education, and use of hormone replacement therapy and oral contraceptives. Follow-up began at baseline and continued until a diagnosis of breast cancer, death, emigration from Victoria or June 30, 2002, whichever came first.

**Dependent Variables**

- Risk of invasive breast cancer
- All women consented access to their medical records, and cancers were ascertained by the Victorian Cancer Registry

**Independent Variables**

- Dietary carbohydrates, glycemic index and glycemic load, and dietary fibre
- Dietary intake assessed using 121-item, self-administered food frequency questionnaire, specifically developed for the MCCS
- Glycemic index values of individual food items were obtained and dietary glycemic load was computed
- Alcoholic beverages were not included in the overall glycemic index

**Control Variables**

- Country of birth
- Total energy intake
- Parity
- Age at first full-term pregnancy
- Cumulative lactation
- Hormone replacement therapy
- Oral contraceptive use
- Age at menarche and menopause
- Maternal family history of cancer
- Physical activity
- Alcohol intake
- Highest level of education
- Height
- Weight
- BMI
- Waist-to-hip ratio

- Multi-vitamin supplement use
- Total fat intake

**Description of Actual Data Sample:**

**Initial N**: 24,479 women in original cohort of 41,528 people

**Attrition (final N):** 324 breast cancers diagnosed in 12,273 postmenopausal women

**Age**: aged 40 - 69 years at baseline

**Ethnicity**: not mentioned

**Other relevant demographics**:

Country of birth:

- 69.8% Australia
- 6.3% United Kingdom
- 13.4% Italy
- 10.5% Greece

**Anthropometrics**

**Location**: Australia

**Summary of Results:**

Adjusted Relative Risks for the Association Between Glycemic Index, Glycemic Load, and Breast Cancer Risk in Localized and Non-Localized Tumours

| | All Cases (n = 324) | Non-localized (n = 127) | Localized (n = 172) | P-value |
|---|---|---|---|---|
| Glycemic index | 0.98 (0.88, 1.10) | 0.99 (0.82, 1.18) | 0.96 (0.83, 1.12) | 0.85 |
| Glycemic load | 1.19 (0.93, 1.52) | 1.07 (0.80, 1.44) | 1.25 (0.95, 1.64) | 0.21 |

**Key Findings**

Altogether, 324 invasive breast cancers were identified during an average of 9.1 years follow-up.

Although an increase of 1 standard deviation in carbohydrate was marginally associated with risk of breast cancer (relative risk = 1.31, 95% confidence interval: 0.98, 1.75), there were no significant associations with fibre (RR = 1.08, 95% confidence interval: 0.92, 1.26), glycemic index (RR = 0.98, 95% confidence interval: 0.88, 1.10) or glycemic load (RR = 1.19, 95% confidence interval: 0.93, 1.52) or with carbohydrate foods (bread, rice, and pasta).

The RR for carbohydrate and localized disease was elevated (RR = 1.40, 95% confidence interval: 1.02, 1.92), but like those for fibre, glycemic index and glycemic load did not differ significantly between localized and non-localized disease.

RRs for grade I, but not grade II or grade III, tumours were elevated for fibre (RR = 1.38, 95% confidence interval: 1.08, 1.75), carbohydrate (RR = 1.56, 95% confidence interval: 1.08, 2.25)

and glycemic load (RR = 1.41, 95% confidence interval: 1.01, 1.98) but not for glycemic index (RR = 0.84, 95% confidence interval: 0.65, 1.09).

The RRs for fibre and estrogen receptor-positive and progesterone receptor-positive tumours (RR = 1.36, 95% confidence interval: 1.10, 1.67), differed significantly from those for estrogen receptor-positive and and progesterone receptor- negative tumours (RR = 1.01, 95% confidence interval: 0.61, 1.69) and estrogen receptor-negative and progesterone receptor-negative tumours (RR = 0.65, 95% confidence interval: 0.43, 0.99), P = 0.005.

**Author Conclusion:**

Our findings suggest a modest association between fibre, carbohydrate, and the incidence of localized, low grade and estrogen receptor-positive/progesterone receptor-positive invasive tumours. Such tumours have a very favourable prognosis, and we consider that our findings are possibly due to increased use of mammographic screening by women who also adhere to a high-fibre, high-carbohydrate dietary pattern, but we do not have any information on the women's screening history with which to test this hypothesis. Our findings do not support either fibre, carbohydrate, glycemic index or glycemic load being associated with the risk of aggressive postmenopausal breast cancer.

***Reviewer Comments:***

*Dietary intake only assessed at baseline. Alcoholic beverages were not included in the overall glycemic index. Authors note the following limitations:*

- *Possibility that the diet may have changed during the follow-up, leading to increased misclassification of long-term exposures, the large measurement errors associated with estimating food and nutrient intakes, and the under-reporting of food and energy intake*
- *Limited statistical power with the small number of cases currently available*
- *Food frequency questionnaire was not designed specifically for glycemic index calculations, and some details are lacking in the description of carbohydrate foods, making it difficult to accurately attribute the glycemic index values*

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***Research Design and Implementation Criteria Checklist: Primary Research***

**Relevance Questions**

| | | |
|---|---|---|
| 1. | Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies) | N/A |
| 2. | Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about? | Yes |
| 3. | Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice? | Yes |

| | | |
|---|---|---|
| 4. | Is the intervention or procedure feasible? (NA for some epidemiological studies) | N/A |

**Validity Questions**

| | | |
|---|---|---|
| **1.** | **Was the research question clearly stated?** | Yes |
| 1.1. | Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified? | Yes |
| 1.2. | Was (were) the outcome(s) [dependent variable(s)] clearly indicated? | Yes |
| 1.3. | Were the target population and setting specified? | Yes |
| **2.** | **Was the selection of study subjects/patients free from bias?** | Yes |
| 2.1. | Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study? | Yes |
| 2.2. | Were criteria applied equally to all study groups? | Yes |
| 2.3. | Were health, demographics, and other characteristics of subjects described? | Yes |
| 2.4. | Were the subjects/patients a representative sample of the relevant population? | Yes |
| **3.** | **Were study groups comparable?** | Yes |
| 3.1. | Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT) | N/A |
| 3.2. | Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline? | N/A |
| 3.3. | Were concurrent controls used? (Concurrent preferred over historical controls.) | N/A |
| 3.4. | If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis? | Yes |
| 3.5. | If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.) | N/A |
| 3.6. | If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")? | N/A |
| **4.** | **Was method of handling withdrawals described?** | Yes |

| | | |
|---|---|---|
| 4.1. | Were follow-up methods described and the same for all groups? | Yes |
| 4.2. | Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.) | Yes |
| 4.3. | Were all enrolled subjects/patients (in the original sample) accounted for? | Yes |
| 4.4. | Were reasons for withdrawals similar across groups? | N/A |
| 4.5. | If diagnostic test, was decision to perform reference test not dependent on results of test under study? | N/A |
| **5.** | **Was blinding used to prevent introduction of bias?** | Yes |
| 5.1. | In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate? | N/A |
| 5.2. | Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.) | Yes |
| 5.3. | In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded? | Yes |
| 5.4. | In case control study, was case definition explicit and case ascertainment not influenced by exposure status? | N/A |
| 5.5. | In diagnostic study, were test results blinded to patient history and other test results? | N/A |
| **6.** | **Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?** | Yes |
| 6.1. | In RCT or other intervention trial, were protocols described for all regimens studied? | N/A |
| 6.2. | In observational study, were interventions, study settings, and clinicians/provider described? | Yes |
| 6.3. | Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect? | Yes |
| 6.4. | Was the amount of exposure and, if relevant, subject/patient compliance measured? | N/A |
| 6.5. | Were co-interventions (e.g., ancillary treatments, other therapies) described? | N/A |
| 6.6. | Were extra or unplanned treatments described? | N/A |
| 6.7. | Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups? | N/A |
| 6.8. | In diagnostic study, were details of test administration and replication sufficient? | N/A |

| | | |
|---|---|---|
| **7.** | **Were outcomes clearly defined and the measurements valid and reliable?** | No |
| 7.1. | Were primary and secondary endpoints described and relevant to the question? | Yes |
| 7.2. | Were nutrition measures appropriate to question and outcomes of concern? | Yes |
| 7.3. | Was the period of follow-up long enough for important outcome(s) to occur? | Yes |
| 7.4. | Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures? | Yes |
| 7.5. | Was the measurement of effect at an appropriate level of precision? | No |
| 7.6. | Were other factors accounted for (measured) that could affect outcomes? | Yes |
| 7.7. | Were the measurements conducted consistently across groups? | N/A |
| **8.** | **Was the statistical analysis appropriate for the study design and type of outcome indicators?** | Yes |
| 8.1. | Were statistical analyses adequately described and the results reported appropriately? | Yes |
| 8.2. | Were correct statistical tests used and assumptions of test not violated? | Yes |
| 8.3. | Were statistics reported with levels of significance and/or confidence intervals? | Yes |
| 8.4. | Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)? | N/A |
| 8.5. | Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)? | Yes |
| 8.6. | Was clinical significance as well as statistical significance reported? | Yes |
| 8.7. | If negative findings, was a power calculation reported to address type 2 error? | No |
| **9.** | **Are conclusions supported by results with biases and limitations taken into consideration?** | Yes |
| 9.1. | Is there a discussion of findings? | Yes |
| 9.2. | Are biases and study limitations identified and discussed? | Yes |
| **10.** | **Is bias due to study's funding or sponsorship unlikely?** | Yes |
| 10.1. | Were sources of funding and investigators' affiliations described? | No |
| 10.2. | Was the study free from apparent conflict of interest? | Yes |